contains cefixime trihydrate equivalent to either 200 milligrams or 400 milligrams of cefixime. Its cefixime trihydrate content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of cefixime that it is represented to contain. Its moisture content is not more than 10.0 percent. It passes the dissolution test. It passes the identity test for the presence of the cefixime moiety. The cefixime used conforms to the standards prescribed by §442.15(a)(1) of this part.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The cefixime used in making the batch for potency, moisture, pH, crystallinity, specific rotation, and identity.

(B) The batch, for content, moisture, dissolution, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research.

(A) The cefixime used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 10 immediate containers.

(b) *Tests and methods of assay*—(1) *Content.* Proceed as directed in §442.15(b)(1) of this part, preparing the sample solution and calculating the cefixime content as follows:

(i) *Preparation of sample solution.* Grind one or a known number of tablets using a mortar and pestle. Quantitatively transfer the ground tablet(s) into a suitable volumetric flask, sonicate and dilute with 0.1*M* phosphate buffer, pH 7.0 to a concentration of 4 milligrams per milliliter. Centrifuge the sample at 3,000 revolutions per minute for 10 minutes. Take an aliquot of the supernatant and qualitatively dilute to a concentration of 0.2 milligram of cefixime activity per milliliter in 0.1*M* phosphate buffer, pH 7.0 (estimated).

(ii) *Calculations.* Calculate the cefixime content as follows:

$$\text{Milligrams of cefixime per tablet} = \frac{A_u \times P_s \times d}{A_s \times n}$$

where:

A_u = Area of the cefixime peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s = Area of the cefixime peak in the chromatogram of the cefixime working standard.

P_s = Cefixime activity in the cefixime working standard solution in micrograms per milliliter;

d = Dilution factor of the sample; and

n = Number of tablets in the sample.

(2) *Moisture.* Proceed as directed in §436.201 of this chapter.

(3) *Dissolution test.* Proceed as directed in §436.215 of this chapter. The quantity Q (the amount of cefixime dissolved) is 75 percent within 45 minutes.

(4) *Identity.* The high-performance liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the cefixime working standard.

[53 FR 24259, June 28, 1988]

§442.119 Cefuroxime axetil oral dosage forms.

§442.119a Cefuroxime axetil tablets.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefuroxime axetil tablets are composed of cefuroxime axetil and one or more suitable and harmless diluents, binders, lubricants, and colorings. Each tablet contains 125 milligrams, 250 milligrams, or 500 milligrams of cefuroxime activity. Its potency is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of cefuroxime activity that it is represented to contain. Its moisture content is not more than 2.0 percent at the time of certification and not more than 6.0 percent at the time of expiry. It passes the dissolution test. It passes the film-coat rupture test. It passes the identity test. The cefuroxime axetil used conforms to the standards prescribed by §442.19(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The cefuroxime axetil used in making the batch for potency, isomer A ratio, moisture, crystallinity, and identity.

(B) The batch for potency, moisture, dissolution, film-coat rupture, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The cefuroxime axetil used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 100 tablets.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 442.19(b)(1). Working standard and sample solutions, system suitability requirements, and calculations are as follows:

(i) *Preparation of working standard and sample solutions*—(A) *Working standard solution.* Dissolve approximately 30 milligrams of the cefuroxime axetil working standard, accurately weighed, in methanol and dilute to 25 milliliters. Transfer 10.0 milliliters of the working standard solution to a 50-milliliter volumetric flask. Add 5.0 milliliters of internal standard solution, 3.8 milliliters of methanol, and dilute to volume with 0.2*M* ammonium phosphate solution to obtain a stock solution containing 0.24 milligram of cefuroxime axetil per milliliter. Store the stock solution under refrigeration no more than 8 hours.

(B) *Sample solution.* Grind a representative number of tablets in a mortar and pestle. Immediately swirl the ground tablets in a volumetric flask containing methanol and shake for 10 minutes to dissolve the ground cefuroxime axetil. Dilute with methanol to give a stock solution of convenient concentration. Filter the stock solution. Transfer 5.0 milliliters of filtrate to a 50-milliliter volumetric flask. Add 5.0 milliliters of internal standard solution and 8.8 milliliters of methanol. Dilute to volume with 0.2*M* ammonium phosphate solution. Store in a refrigerator and use within 8 hours.

(ii) *System suitability requirements*—(A) *Tailing factor.* The tailing factor (*T*) is satisfactory for isomer A if it is not more than 1.5 at 5 percent of peak height.

(B) *Efficiency of the column.* The efficiency of the column (*n*) is satisfactory for isomer A if it is greater than 3,000 theoretical plates.

(C) *Resolution.* The resolution (*R*) between isomer A and isomer B of cefuroxime axetil is satisfactory if it is not less than 1.5 and the resolution (*R*) between isomer A and the delta-2 isomers of cefuroxime axetil is satisfactory if it is not less than 1.5.

(D) *Coefficient of variation.* The coefficient of variation (S_R in percent) of five replicate injections is not more than 2.0 percent. If the system suitability requirements have been met, then proceed as described in § 436.216(b) of this chapter. Alternate chromatographic conditions are acceptable provided reproducibility and resolution are comparable to the system. However, the sample preparation described in paragraph (b)(1)(i)(B) of this section should not be changed.

(iii) *Calculations.* Calculate the cefuroxime content as follows:

$$\text{Milligrams of cefuroxime per tablet} = \frac{R_u \times P_s \times d}{R_s \times n}$$

where:

R_u=Sum of the peak heights of the cefuroxime axetil sample isomer A and isomer B peaks/Peak height of the internal standard;

R_s=Sum of the peak heights of the cefuroxime axetil working standard isomer A and isomer B peaks/Peak height of the internal standard;

P_s=Potency of the cefuroxime axetil working standard in milligrams of cefuroxime activity per milliliter;

d=Dilution factor of the sample; and

n=Number of tablets in the sample assayed.

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter, using the titration procedure described in paragraph (e)(1) of that section.

(3) *Dissolution.* Proceed as directed in § 436.215 of this chapter. The quantity *Q* (the amount of cefuroxime activity dissolved) is 60 percent at 15 minutes and 75 percent at 45 minutes.

(4) *Film-coat rupture test.* Proceed as directed in §436.217 of this chapter.

(5) *Identity.* The high-performance liquid chromatogram of the sample solution determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the cefuroxime axetil working standard solution.

[52 FR 42433, Nov. 5, 1987; 52 FR 45528, Nov. 30, 1987, as amended at 54 FR 47352, Nov. 14, 1989; 54 FR 50472, Dec. 6, 1989; 55 FR 11583, Mar. 29, 1990. Redesignated at 60 FR 27222, May 23, 1995]

§442.119b Cefuroxime axetil for oral suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefuroxime axetil for oral suspension is cefuroxime axetil with one or more suitable and harmless diluents, suspending and sweetening agents, and flavorings. When reconstituted as directed in the labeling, it contains cefuroxime axetil equivalent to 25 milligrams of cefuroxime per millimeter. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of cefuroxime that it is represented to contain. It passes the dissolution test. Its moisture content is not more than 0.2 percent. When reconstituted as directed in the labeling, its pH is not less than 3.5 and not more than 5.5. It passes the identity test. The cefuroxime axetil used conforms to the standards prescribed by §442.19(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The cefuroxime axetil used in making the batch for potency, isomer A ratio, moisture, crystallinity, and identity.

(B) The batch for cefuroxime potency, dissolution, moisture, pH of constituted suspension, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The cefuroxime axetil used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 12 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in §442.19(b)(1). Working standard and sample solutions and calculations are as follows:

(i) *Preparation of working standard solution.* Dissolve approximately 15 milligrams of the cefuroxime axetil working standard, accurately weighed, in 20.0 milliliters of methanol in a 50-milliliter volumetric flask. Dilute to volume with deionized water, and swirl to mix. Store for no more than 8 hours under refrigeration and protected from light.

(ii) *Preparation of sample solution.* Reconstitute the sample as directed in the labeling. Transfer an accurately measured representative portion of the suspension equivalent to one dose into a 200-milliliter volumetric flask. Add 10 milliliters of methanol and disperse the sample. Dilute to volume with methanol. Dilute 20.0 milliliters of this solution to volume in a 50-milliliter volumetric flask with deionized water, swirl to mix, and allow to stand for 10 minutes. (Note: A white turbidity is formed.) Filter this solution via a suitable disposable filter unit, discarding the first 5 milliliters. Store for no more than 8 hours under refrigeration and protect from light.

(iii) *Calculations.* Calculate the milligrams of cefuroxime per dose (5 milliliters) as follows:

$$\text{Milligrams of cefuroxime per 5 milliliters of sample} = \frac{A_U \times P_S \times d}{A_S \times 1{,}000}$$

where:

A_U = Sum of the areas of the cefuroxime axetil sample isomer A and isomer B peaks;

A_S = Sum of the peak areas of the cefuroxime axetil working standard isomer A and isomer B peaks;

P_S = Cefuroxime activity in the cefuroxime axetil working standard solution in micrograms per milliliter; and

d = Dilution factor of the sample.

(2) *Dissolution.* Proceed as directed in §436.215 of this chapter. The quantity Q (the amount of cefuroxime activity dissolved) is 60 percent at 30 minutes.